Published in final edited form as:
Ann Surg. 2017 August ; 266(2): 353–360. doi:10.1097/SLA.0000000000001972.

Rising Bilateral Mastectomy Rates Among Neoadjuvant Chemotherapy Recipients in California, 1998–2012

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Abstract

Background—Neoadjuvant chemotherapy (NAC) for operable breast cancer (BC) can downstage disease and facilitate breast conservation.

Objective—To assess trends in NAC use and surgical procedures in California from 1/1/1998 to 12/31/2012 using statewide population-based cancer registry data.

Methods—236,797 women diagnosed with stage I–III BC were studied. Information regarding NAC, adjuvant chemotherapy (aCT), breast conserving surgery (BCS), bilateral mastectomy (BLM) and unilateral mastectomy (ULM) was abstracted from the medical records. Multivariable polytomous logistic regression were used to estimate odds ratios (OR) of receiving NAC and of type of surgery after NAC.

Results—40.1% (94,980) of patients received chemotherapy: 87% (82,588) aCT and 13.0% (12,392) NAC. NAC use more than doubled over time and increased with stage (Stage I, 0.7%; Stage III, 29.9%). Multivariable predictors of NAC treatment were stage (III), younger age (<40 years), Black or Hispanic race/ethnicity [versus non-Hispanic-white, OR 1.10, 95% confidence interval (CI) 1.05–1.16], and care at a National Cancer Institute (NCI)-designated center (OR 1.70, CI 1.58–1.82). Most (68.4%) NAC recipients had mastectomies, and 14.3% of them underwent BLM. In contrast, 47.9% aCT patients had mastectomies with 7.3% BLM. The only independent predictor of BCS after NAC was care at a NCI-designated center (OR 1.28, CI 1.10–1.49), and of BLM, age <40 (vs. 50–64, OR 2.59, CI 2.21–3.03), or residence in the highest socioeconomic neighborhood quintile (vs. lowest, OR 2.10, CI 1.67–2.64).

Conclusion—NAC use remains low. Predictors of surgery type after NAC were sociodemographic rather than clinical, raising concern for disparities in care access.

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Prior Publication: A portion of this manuscript was presented in poster form at the Annual Meeting of the American Society of Clinical Oncology, Chicago, IL, June 3–6, 2016.

INTRODUCTION

The benefits of neoadjuvant chemotherapy (NAC) for breast cancer are multifaceted: providing insight into chemosensitivity, facilitating breast conservation, and delivering unique prognostic information. NAC use is on the rise as reflected in recent statistics from the National Cancer Database [1]. Long-term follow-up has shown consistent and equivalent overall survival between adjuvant (postoperative) chemotherapy (aCT) and NAC treatment groups, proving that surgical delay for systemic therapy is not detrimental. Moreover, NAC provides an *in vivo* test that discriminates between treatment responders and non-responders, and yields unique prognostic information based on residual cancer burden [2]. Furthermore, re-evaluation of tumor biomarkers or genomic profiling may guide post-NAC therapies.

A practical aspect of NAC is disease down-staging. Lumpectomy use increased by 12% in the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-18 protocol, the first randomized comparison of aCT to NAC in palpable, operable breast cancer [3]. These observations have since been corroborated in a subsequent pooled analysis [4]. Moreover, initiating chemotherapy before surgery has been associated (albeit non-significantly) with better survival in younger women (aged <50 years at diagnosis) [5]. As the neoadjuvant approach has gained acceptance, surgeons and radiation oncologists have been challenged to adapt the use of sentinel node biopsy, and to reconsider regional radiation in this patient population [6–10]. Another benefit of NAC is that it enables faster evaluation of drug regimens compared to the same treatments given adjuvantly. Consequently, the United States Food and Drug Administration (FDA) recently accepted tumor response to NAC as a drug approval endpoint, with pertuzumab the first agent thus approved [4, 11, 12].

Implementing NAC requires multidisciplinary coordination between surgeons and medical oncologists at the time of initital diagnosis and therefore its prevalence in mainstream practice is largely unknown. We and others recently reported a substantial rise in use the use of bilateral mastectomy (BLM, unilateral therapeutic with contralateral prophylactic mastectomy) for early-stage breast cancer [13–16]. However, the use of BLM among NAC-treated patients has not been studied, nor has the question of whether disease down-staging translates into a greater use of breast conserving surgery (BCS). Our objective was to characterize the use of NAC in a real-world, population-based setting, and to examine the use and correlates of subsequent breast surgical procedures after NAC (e.g., BLM, BCS and ULM). To achieve this objective, we took advantage of the population-based California Cancer Registry [CCR, contributing registries to the Surveillance, Epidemiology and End Results (SEER) Program], which collects data on cancer incidence, clinical or pathological stage of disease, surgical intervention and the first course of treatment.

METHODS

Case Ascertainment and Data Collection

The study population included all female California residents diagnosed with a first primary breast cancer of American Joint Commission on Cancer (AJCC) stages I–III from January 1, 1998 through December 31, 2012. International Classification of Diseases for Oncology, third edition (ICD-0-3) site codes C50.0–C50.9 were used excluding any breast tumors with hematopoietic, mesothelioma, or Kaposi's sarcoma histologic codes (ICD-O-3 morphology codes 9050–9055, 9140, 9590–9992). This human subject research was approved as part of the Cancer Prevention Institute of California Institutional Review Board's cancer registry protocol. We used CCR data routinely abstracted from medical records regarding patient age at diagnosis, race/ethnicity, marital status, stage, tumor grade, size and histology; lymph node involvement, metastasis, tumor molecular markers including estrogen receptor, progesterone receptor and HER2, first course of treatment (surgery, chemotherapy including its timing in relation to surgery, and radiation therapy), primary health insurance, and residence (Census block group) at diagnosis [17].

Tumor and Lymph Node Staging

According to SEER protocol, AJCC stage is derived from reported tumor size (T), lymph node (N) and metastasis (M) components [17]. From 1998–2003, clinical tumor size (T) was reported for NAC recipients (clinical staging). Nodal status, however, was represented by the highest reported N stage at any time. For example, node-negative status by pathologic staging after surgery would be entered according to the higher clinical staging if nodes were involved before NAC [17]. In the timeframe of 2004–2012, both T and N were the highest stage reported, and the distribution of staging method among NAC-treated patients is shown in the Supplemental Table. Stage assigned corresponds to the AJCC 3rd edition for cases diagnosed 1998–2003, 6th edition for cases diagnosed 2004–2009 and the 7th edition for cases diagnosed 2010–2012.

Neighborhood-Level Information

We used a previously developed measure of the neighborhood socioeconomic status (nSES) based on patients' residence at the time of cancer diagnosis. For cases diagnosed in 1998–2005, this measure comprised quintiles based on the statewide distribution of census block groups from the 2000 Census on education, housing costs, income and occupation [18]. For cases diagnosed in 2006–2012, we used the 2007–2011 American Community Survey of the U.S. Census [19]. Urban-rural designation at the medical service study area (MSSA) based on the 2000 and 2010 Census was included.

Hospital-Level Information

The CCR records the institution that first reports each cancer case, which is the treating facility for the great majority (94.8%) of cases [17]. For each facility, we determined the nSES distribution of all cases, and identified facilities that were NCI-designated cancer centers.

Statistical Analysis

We used multivariable logistic regression to estimate adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for the association of patient, tumor, sociodemographic, and facility characteristics with receipt of NAC (versus no receipt of NAC). The following variables were included in the model: age; race/ethnicity; diagnosis year; stage; histology; grade; lymph node involvement; hormone receptor status; marital status; primary insurance; nSES; the reporting hospital's NCI-designation status and nSES distribution of patients. As

HER2 data were missing in 41% of cases diagnosed before 2005, we constructed a model including HER2 status, limited to patients for whom it was known. Polytomous logistic regression was used to model surgical procedure after NAC, with unilateral mastectomy as the referent procedure. All analyses were conducted using SAS 9.3 (Cary, North Carolina).

RESULTS

Patient Characteristics

A total of 253,986 stage I–III breast cancer cases were diagnosed and reported to CCR from January 1, 1998 to December 31, 2012, of which 236,797 were considered eligible (Supplemental Figure 1). Patients with a metachronous contralateral breast cancer (N=5,690, 2.4%) were not excluded; however, only the breast surgery undertaken for treatment of the first cancer was analyzed and in the case of mastectomy, was counted as a ULM. BLMs reported here pertain only to mastectomy treatment for the cancer-affected breast with a contralateral prophylactic mastectomy (CPM). For patients diagnosed from 2004–2012, T and N staging (the highest stage reported, as described above) was clinical in 63.9% and pathologic in 36.1%.

Use of Chemotherapy, NAC and aCT

Among all analyzed patients, 141,817 (59.9%) received no chemotherapy, 82,588 (34.9%) aCT, and 12,392 (5.2%) NAC (Tables 1–2). Considering only chemotherapy recipients (N=94,980), 87.0% received aCT and 13.0% NAC. The proportion of patients treated with NAC increased noticeably from 7.9% in 1998 to 18.0–20.0 % in 2011–2012 (Figure 1). The ratio of aCT to NAC among chemotherapy recipients was inversely related to stage (Stage I: 96.6% aCT and 3.4% NAC; Stage II: 89.0% aCT and 11.0% NAC; Stage III: 70.1% aCT and 29.9% NAC). Similar trends are are reflected by tumor size and number of involved nodes (Table 2).

NAC was used in 8.8% of uninsured or self-pay, 7.1% of public/Medicaid and 1.9% of Medicare-insured patients. Public/Medicaid-insured patients had the highest proportional use of NAC (19.1%), followed by 17.9% for not insured/self-pay, 14.2% for military, 11.7% for private and 10.3% for Medicare. Excluding Medicare patients, the use of no chemotherapy (as compared to the other options of NAC and aCT) was highest at 62.8% among public/Medicaid insured patients. Use of NAC, aCT and no chemotherapy also varied by age (Figure 2). Over time, chemotherapy use decreased slightly in the 40–49 and 50–64 age groups, while increasing in the 65 and older cohort and most notably in women under the age of 40.

Use of Surgical Procedures after NAC

Overall, 41.5% of all women treated during this study period underwent either ULM or BLM (Table 2). However, the mastectomy rate was higher (50.6%) for the 94,980 patients treated with systemic chemotherapy and 16.4% of these were bilateral. The most common surgical procedure after NAC was ULM (6702, 54.1%), followed by BCS (31.6%), although there was an increase in the latter over time (Figure 3). BLM rates were highest among NAC recipients:14.3%, compared to 7.3% of aCT and 4.3% of the no chemotherapy subgroups.

Mastectomy after aCT was performed in 47.9% cases, of which 15.9% were BLM. Surgical procedure use also varied by age (Supplemental Figure 2).

Independent Predictors of Neoadjuvant Chemotherapy Use

On multivariable analysis, factors significantly associated with receiving NAC (Figure 4) included younger age [<40 versus 50–64 years: OR 1.97, CI 1.865–2.0910], more recent diagnosis, higher stage (III versus I: OR 32.657, CI 29.8078–35.8279), higher grade, and ER/PR-negative status. To address the missing data on HER2, a crucial treatment biomarker, a sensitivity analysis was performed including only cases with known HER2 status. Reassuringly, similar results were noted for the whole cohort. In a model limited to cases of known HER2 status, HER2-positivity was significantly associated with receipt of NAC (OR 1.56, CI 1.47–1.65, data not shown).

Ethnicity and race were not factors in NAC use except for small effects among Hispanics versus Non-Hispanic (NH) white, [OR 1.0910, CI 1.035–1.156] and NH Black vs. NH White (OR 1.09, CI 1.01–1.18). NAC treatment was also associated with unmarried status, public/Medicaid insurance or lack of insurance, and care at a NCI-designated cancer center (OR 1.6970, CI 1.58–1.82), and inversely associated with residence in a rural versus urban MSSA and care at a hospital with proportionally more lower SES patients.

Independent Predictors of Surgical Treatment Use after Neoadjuvant Chemotherapy

On multivariable analysis (Table 3), the only factors independently associated with having BCS instead of ULM after NAC were care at an NCI-designated cancer center (OR 1.28, CI 1.10–1.49), and more recent diagnosis. Factors independently associated with receiving BLM instead of ULM after NAC were young age (<40 versus 50–64 years: OR 2.59, CI 2.21–3.03), high nSES (top versus bottom quintile: OR 2.10, CI 1.67–2.64), and more recent time period of diagnosis (2012 versus 1998: OR 8.66, CI 5.38–13.9).

DISCUSSION

In the large, diverse population of California, overall use of NAC among breast cancer patients who received chemotherapy increased steadily over time to 18–20% in 2011–2012 and was highly associated with the age of patients. These observations are consistent with recent studies of the National Cancer Database (NCDB) that reported 17–23% NAC use among chemotherapy recipients [1, 20, 21]. We found that greater NAC use was also associated with NCI-designated cancer centers. Our most striking finding was that NAC recipients had higher rates of BLM than did patients with comparable prognostic factors. Arguments in favor of NAC include earlier initiation of systemic treatments to address micrometastatic disease, as well as down-staging of tumor in the breast and axillary nodes [8, 10, 22]. A decision to undergo CPM, in addition to ULM, runs counter to one of NAC's primary benefits: to preserve the breast. Moreover, the higher cancer stage among most NAC patients (compared to aCT patients and those not treated with chemotherapy) suggests that development of distant metastasis is a greater risk than developing a metachronous contralateral primary cancer. Our results raise questions about which goals drive NAC use in the real-world setting, and warrant further investigation of the quality of such care.

Other studies have investigated patterns of NAC use, most recently in the NCDB; the authors reported a similar NAC rate as we observed, and also found statewide variation in NAC use (with California approximately in the middle among all states). Our findings of greater NAC use by young patients, racial/ethnic minorities, and academic centers are also consistent with prior studies [20, 21]. Our current study contributes a novel, real-world view of NAC utilization and subsequent surgical procedures, taking advantage of the CCR's comprehensive recording of >99% of cancer cases in the nation's most populous, most racially/ethnically diverse state. Consistent with practice guidelines, NAC use increased with cancer stage and adverse prognostic factors. Surprisingly, low SES, including residence in a low SES neighborhood, diagnosis in a hospitals with greater prorportion of lower SES patients, and having public/Medicaid insurance, were associated with more NAC use, perhaps consistent with a propensity for later-stage presentation or biologically more aggressive disease. Lower NAC use among patients in rural regions may reflect lower access to facilities performing NAC and/or difficulty with repeated travel to a hospital for care. Predictably, NCI-designated centers had higher NAC use, consistent with their mission of innovation, clinical trial participation and adoption of new guidelines [11, 12].

NAC was first developed for advanced breast cancer cases. The use of breast conservation after disease down-staging with NAC was addressed in the seminal neoadjuvant therapy trial, NSABP B-18 [3]. A recent NCDB study found a correlation between NAC use and BCS, although only among tumors larger than 3 cm [1]. By contrast, we found that the predictors of receiving either BCS or BLM (rather than the most common surgical procedure, ULM) after NAC were not clinical cancer prognostic factors but instead were the sociodemographic characteristics of patients and hospitals. Other than more recent diagnosis, the sole predictor of post-NAC BCS was care at a NCI-designated cancer center, and the predictors of post-NAC BLM were younger age and high neighborhood SES. These results indicate that post-NAC surgical decisions were influenced by non-clinical factors (e.g., age, NCI-designation status and neighborhood SES).

Our finding that post-NAC surgery was primarily associated with sociodemographic and hospital factors also prompts questions about care variability in different settings, available specialty services, and whether patients are uniformly presented with all available treatment options. For example, lower rates of BCS after NAC were recorded at non-NCI-designated cancer centers. This may indicate persistent conservative management attitudes at such centers, with surgeons favoring mastectomy for patients presenting with large palpable tumors, especially T3 lesions. Moreover, surgeons have disagreed on whether the entire tumor bed should be resected after NAC (which would favor more extensive surgery) or whether resection should focus only on the residual disease.

CPM, not an increase in synchronous bilateral breast cancer, accounts for the notable rise in BLM rates reported in this study and others [15, 16]. In the case of BLM, the CCR lacks data on how often post-mastectomy reconstruction was employed, a metric which could inform understanding of the sophistication and services available in treating facilities. Many explanations have been proposed for rising BLM rates, ranging from fear of a second cancer to a preference for cosmetic symmetry that BLM may best enable [23]. Despite its rising use, however, CPM does not reduce mortality in most patients [16]. Our findings thus identify BLM use after NAC as a potential target for initiatives to improve the quality of breast cancer care. An important step towards quality improvement will be to determine whether there is any survival benefit of one surgical procedure over another (BCS vs. ULM vs. BLM) among complete versus partial responders to NAC.

Several factors warrant consideration in interpreting our results. Notably, SEER reports only the highest stage. Therefore, the recorded stage for NAC recipients is usually clinical (before any treatment) as it was in 63.8% of our cases, while for those who receive surgery before systemic therapy the recorded stage is usually pathological. This systematic difference in staging method between aCT and NAC patients may introduce bias. For one Given SEER's protocol for stage reporting, it is not possible to identify cases that were down-staged by the use of NAC, nor to determine whether the the degree of response to NAC is associated with the choice of surgical procedure. It is reassuring, however, that the proportion of patients treated with NAC that we report here was similar to data from NCDB which does distinguishes between methods and timing of staging [1]. Another limitation is that prevalence of family cancer history and *BRCA1/2* mutations are not collected by cancer registries; these factors clearly influence decisions in favor of BLM. Further limitations are the lack of information on tumor response to NAC, which could be corrected by adoption of clinically relevant yp staging criteria across SEER registries [24], and the absence of patient-reported and physician-reported data on the opinions that shaped treatment decisions. Our work has several notable strengths. California is the most populous and diverse state in the nation, and NAC usage falls in the middle among U.S. regions [21]. Since the population-based CCR encompasses all of California, selection bias was minimized and our results have broad relevance. Using CCR data allowed us to examine additional patient, hospital, and neighborhood characteristics that are unavailable from other population-based U.S. cancer registry datasets.

In conclusion, the rate of BLM increased nearly four-fold in California over the 15 years of our study period, while NAC use tripled. The FDA's recent endorsement of NAC as a tool to measure drug effectiveness and as a surrogate for systemic response is likely to increase NAC use [11, 12]. How these changing patterns in the timing of systemic therapy affect future surgical treatments should be monitored, particularly as we found that sociodemographic characteristics of patients and hospitals, not clinical prognostic factors, were the primary predictors of surgery type after NAC. This association of post-NAC surgery with social rather than clinical factors raises concern for societal disparities in access to different surgical options. The impact of surgical procedures on survival and other clinically relevant outcomes after NAC must be studied, as a step toward quality improvement in the use of NAC and subsequent surgery for early-stage breast cancer.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This study was supported by the Jan Weimer Junior Faculty Chair in Breast Oncology, the Suzanne Pride Bryan Fund for Breast Cancer Research at Stanford Cancer Institute, by the National Cancer Institute's Surveillance, Epidemiology and End Results Program under contract HHSN261201000140C awarded to the Cancer Prevention Institute of California, and by the Stanford Cancer Institute. The collection of cancer incidence data used in this study was supported by the California Department of Health Services as part of the statewide cancer reporting program mandated by California Health and Safety Code Section 103885; the National Cancer Institute's Surveillance, Epidemiology, and End Results Program under contract HHSN261201000140C awarded to the Cancer Prevention Institute of California, contract HHSN261201000035C awarded to the University of Southern California, and contract HHSN261201000034C awarded to the Public Health Institute; and the Centers for Disease Control and Prevention's National Program of Cancer Registries, under agreement #1U58 DP000807-01 awarded to the Public Health Institute. The ideas and opinions expressed herein are those of the authors, and endorsement by the University or State of California, the California Department of Health Services, the National Cancer Institute, or the Centers for Disease Control and Prevention or their contractors and subcontractors is not intended nor should be inferred. None of the funders had any role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; or preparation, review, or approval of the manuscript. Irene L. Wapnir, Allison W. Kurian and Scarlett L. Gomez had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. All authors declare no conflicts of interest.

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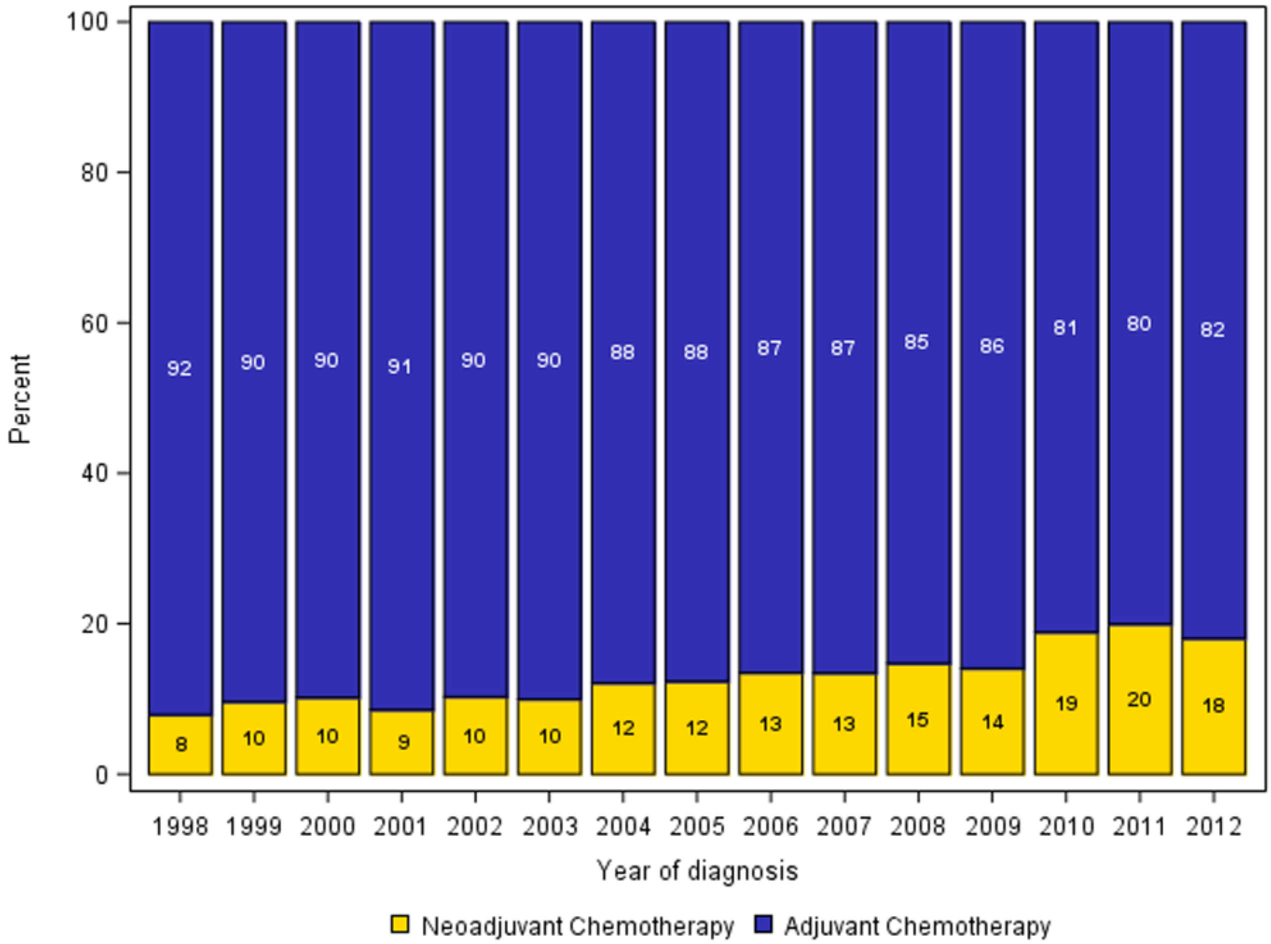

Figure 1.
Usage trends over time of adjuvant chemotherapy (aCT) and neoadjuvant chemotherapy (NAC) limited to recipients of chemotherapy

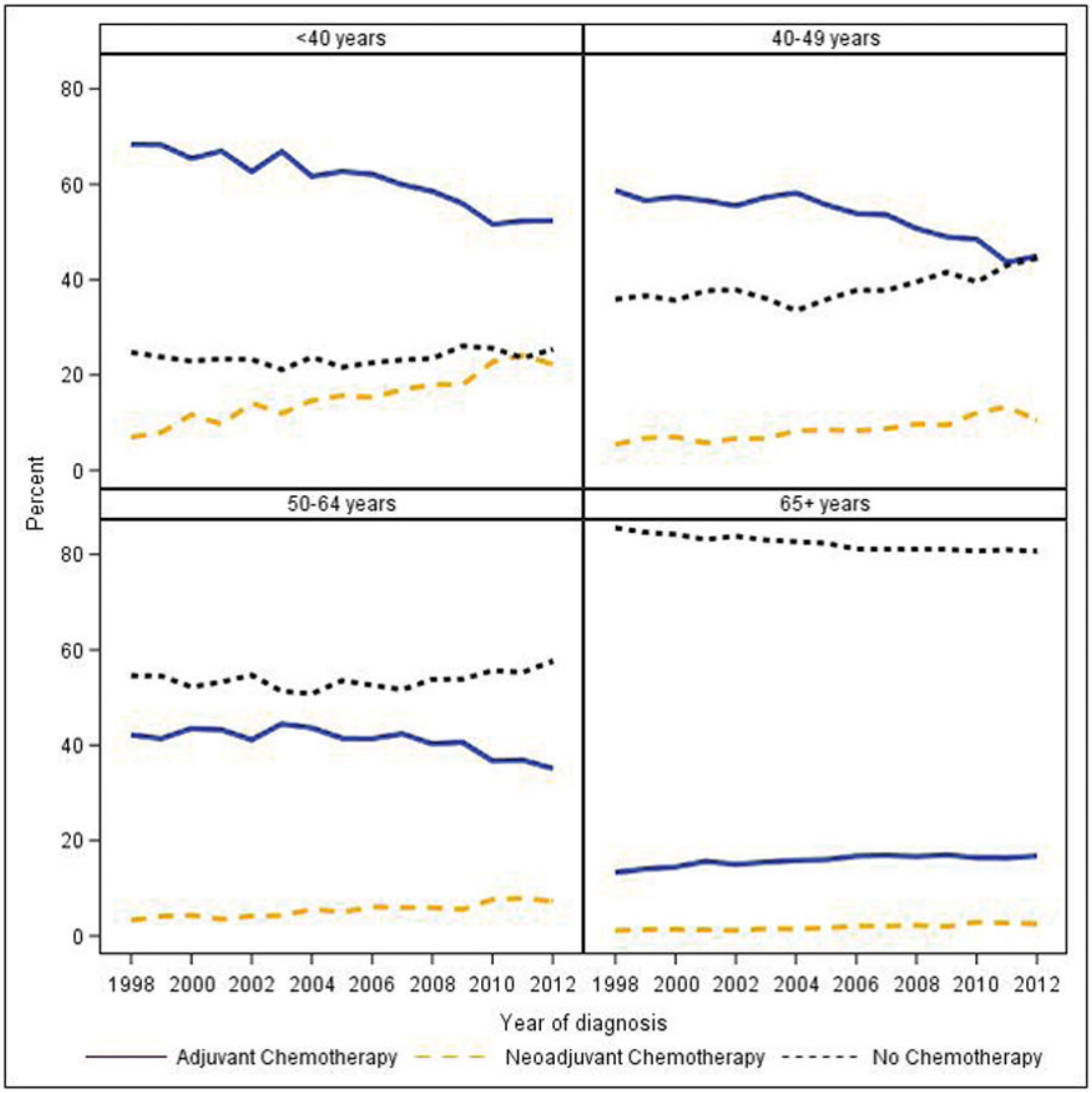

Figure 2.

Usage trends by age of chemotherapy scenarios (adjuvant chemotherapy (aCT), neoadjuvant chemotherapy (NAC), no chemotherapy, 1998–2012, California

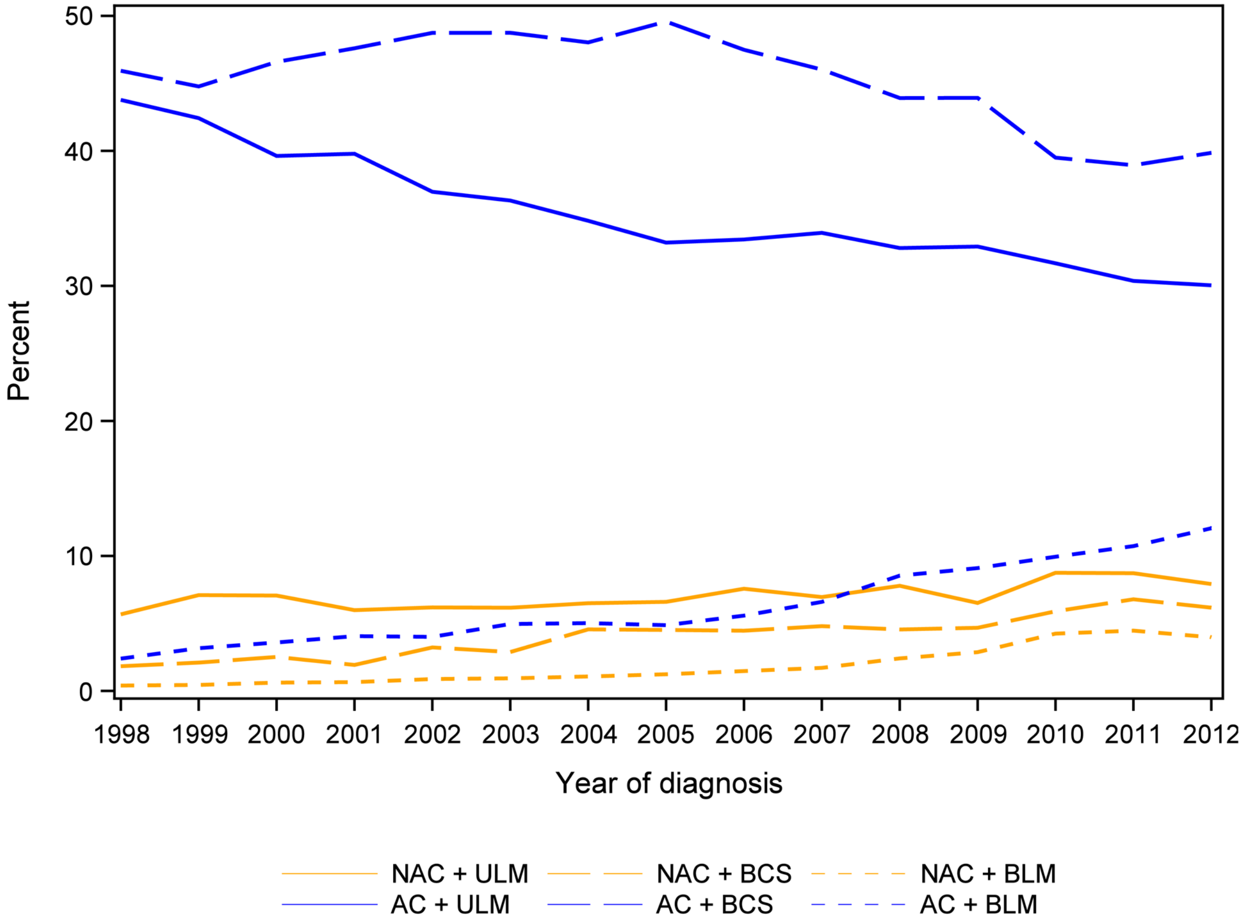

Figure 3.

Usage trends over time of surgical treatments (BCS, breast conserving surgery; BLM, bilateral mastectomy; ULM, unilateral mastectomy) in specific chemotherapy scenarios: adjuvant chemotherapy (aCT), neoadjuvant chemotherapy (NAC), no chemotherapy

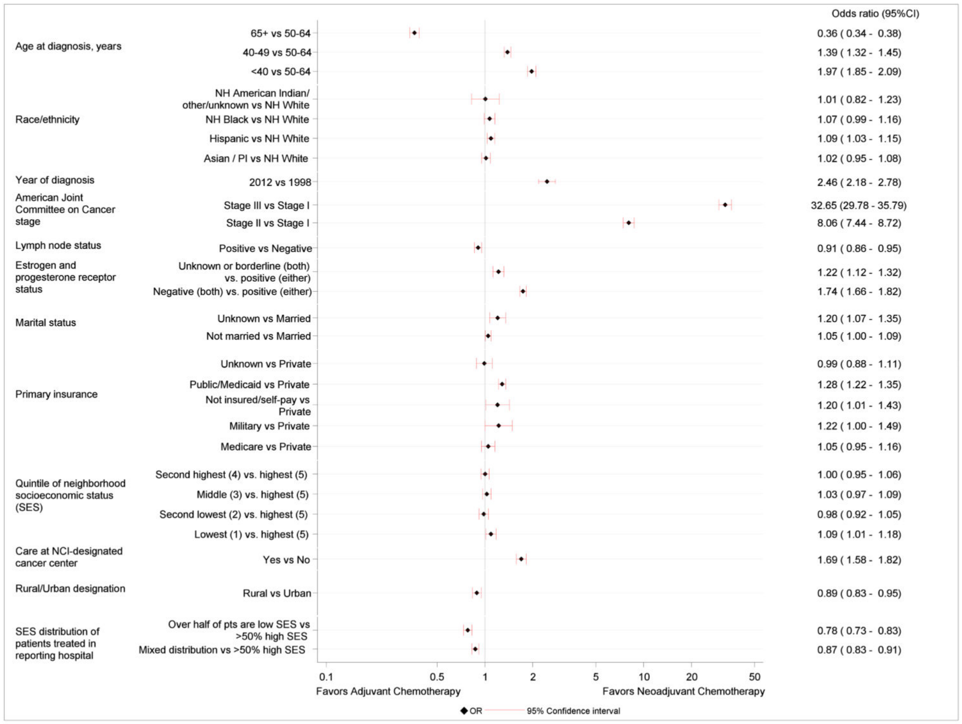

Figure 4.

Multivariable model of factors associated with neoadjuvant chemotherapy use.

Table 1

Distribution of patient sociodemographic factors by timing of chemotherapy: 1998–2012, California

	All Patients N= 236,797	Adjuvant Chemotherapy N= 82,588 (34.9%)		Neoadjuvant Chemotherapy N= 12,392 (5.2%)		No Chemotherapy N= 141,817 (59.9%)	
Age at diagnosis, years							
<40	13,267	8103	61.1%	2031	15.3%	3133	23.6%
40–49	44,999	23960	53.2%	3847	8.5%	17,192	38.2%
50–64	89,453	36473	40.8%	4894	5.5%	48,086	53.8%
≥65	89,078	14052	15.8%	1620	1.8%	73,406	82.4%
Race/Ethnicity							
Non-Hispanic (NH) White	157,264	50086	31.8%	6582	4.2%	100,596	4.2%
NH Black	13,610	5607	41.2%	1040	7.6%	6963	7.6%
Hispanic	37,703	15960	42.3%	3067	8.1%	18,676	8.1%
Asian / Pacific Islander	25,999	10249	39.4%	1580	6.1%	14,170	6.1%
NH American Indian, other or unknown	2221	686	30.9%	123	5.5%	1412	5.5%
Marital status							
Not currently married	94,866	28085	29.6%	4919	5.2%	61,862	65.2%
Married	135,934	52659	38.7%	7078	5.2%	76,197	56.1%
Unknown	5997	1844	30.7%	395	6.6%	3758	62.7%
Quintile of neighborhood socioeconomic status (SES)							
1 (Lowest quintile of SES, based on statewide measure)	26,955	9791	36.3%	1971	7.3%	15,193	56.4%
2	39,552	13916	35.2%	2180	5.5%	23,456	59.3%
3	48,743	16776	34.4%	2520	5.2%	29,447	60.4%
4	56,349	19496	34.6%	2752	4.9%	34,101	60.5%
5 (Highest quintile of SES, based on statewide measure)	65,198	22609	34.7%	2969	4.6%	39,620	60.8%
Primary insurance coverage							
Not insured or self-pay	2016	816	40.5%	178	8.8%	1022	50.7%
Private	148,188	59,232	40.0%	7884	5.3%	81,072	54.7%
Public/Medicaid	44,698	13,450	30.1%	3175	7.1%	28,073	62.8%
Medicare	32,697	5506	16.8%	634	1.9%	26,557	81.2%

	All Patients N= 236,797	Adjuvant Chemotherapy N= 82,588 (34.9%)		Neoadjuvant Chemotherapy N= 12,392 (5.2%)		No Chemotherapy N= 141,817 (59.9%)	
Military	1948	833	42.8%	126	6.5%	989	50.8%
Unknown	7250	2751	37.9%	395	5.4%	4104	56.6%
Care at National Cancer Institute-designated center							
No	224,919	77,894	34.6%	11,212	5.0%	135,813	60.4%
Yes	11,878	4694	39.5%	1180	9.9%	6004	50.5%
SES distribution of patients treated in reporting hospital							
>50% high SES	119,977	41,482	34.6%	6242	5.2%	72,253	60.2%
>50% low SES	43,748	15,940	36.4%	2516	5.8%	25,292	57.8%
Mixed SES distribution							
MSSA-level urban/rural designation	73,072	25,166	34.4%	3634	5.0%	44,272	60.6%
Urban	204,907	71,662	35.0%	11,023	5.4%	122,222	59.6%
Rural (includes frontier and rural)	31,890	10,926	34.3%	1369	4.3%	19,595	61.4%

Table 2

Distribution of tumor and treatment factors by timing of chemotherapy: 1998–2012, California

	All Patients N= 236,797	Adjuvant Chemotherapy N= 82,588		Neoadjuvant Chemotherapy N= 12,392		No Chemotherapy N= 141,817	
American Joint Committee on Cancer stage							
I	119,915	21576	18.0%	824	0.7%	97,515	81.3%
II	92,662	47763	51.5%	5929	6.4%	38,970	42.1%
III	24,220	13249	54.7%	5639	23.3%	5332	22.0%
Tumor size, centimeters (cm)							
Microscopic foci	3389	270	8.0%	26	0.8%	3093	91.3%
<2 cm	131,835	32957	25.0%	1557	1.2%	97,321	73.8%
2–5 cm	86,304	42813	49.6%	6198	7.2%	37,293	43.2%
>5 cm or diffuse	15,269	6548	42.9%	4611	30.2%	4110	26.9%
Number of lymph nodes involved by cancer							
0	148,918	36,779	24.7%	4529	3.0%	107,610	72.3%
1–3	50,492	29,242	57.9%	3798	7.5%	17,452	34.6%
≥4	23,975	15,525	64.8%	3264	13.6%	5186	21.6%
Number unknown	13,412	1042	7.8%	801	6.0%	11,569	86.3%
Estrogen and progesterone receptor (ER, PR) status							
ER and PR both negative	38,642	21,589	55.9%	4287	11.1%	12,766	33.0%
ER and/or PR positive	178,033	56,880	31.9%	7225	4.1%	113,928	64.0%
ER and/or PR unknown or borderline	20,122	4119	20.5%	880	4.4%	15,123	75.2%
HER2 status							
Negative	142,618	47,743	33.5%	6931	4.9%	87,944	61.7%
Positive	32,045	16,784	52.4%	3255	10.2%	12,006	37.5%
Unknown or borderline	62,134	18,061	29.1%	2206	3.6%	41,867	67.4%
Radiation therapy							
Not received	117,509	36,789	31.3%	5023	4.3%	75,697	64.4%
Received	119,288	45,799	38.4%	7369	6.2%	66,120	55.4%
Surgical procedure	84,369	33,505	39.7%	6702	7.9%	44,162	52.3%

	All Patients N= 236,797	Adjuvant Chemotherapy N= 82,588		Neoadjuvant Chemotherapy N= 12,392		No Chemotherapy N= 141,817	
Unilateral mastectomy							
Bilateral mastectomy	13,899	6089	43.8%	1775	12.8%	6035	43.4%
Breast conserving surgery	138,529	42,994	31.0%	3915	2.8%	91,620	66.1%

Table 3

Multivariable model of factors associated with surgical procedure among recipients of neoadjuvant chemotherapy

Variable	Comparison groups	Breast conserving surgery (BCS) versus unilateral mastectomy (ULM) OR (95% CI)*	Bilateral mastectomy (BLM) versus ULM OR (95% CI)*
Age at diagnosis, years	<40 versus (vs.) 50–64	0.85 (0.74 – 0.97)	2.59 (2.21 – 3.03)
	40–49 vs. 50–64	1.06 (0.95 – 1.18)	1.64 (1.43 – 1.88)
	≥65 vs. 50–64	0.67 (0.57 – 0.78)	0.56 (0.44 – 0.71)
Race/Ethnicity	Asian/Pacific Islander vs. Non-Hispanic (NH) White	0.58 (0.50 – 0.67)	0.47 (0.39 – 0.57)
	Hispanic vs. NH White	0.77 (0.68 – 0.87)	0.61 (0.52 – 0.72)
	NH American Indian, other or unknown vs. NH White	0.98 (0.63 – 1.53)	1.01 (0.59 – 1.72)
	NH Black vs. NH White	0.83 (0.70 – 0.99)	0.60 (0.47 – 0.77)
American Joint Committee on Cancer stage	Stage II vs. Stage I	0.71 (0.59 – 0.85)	0.63 (0.49 – 0.80)
	Stage III vs. Stage I	0.17 (0.14 – 0.21)	0.42 (0.32 – 0.55)
Estrogen and progesterone receptor status	Negative (both) vs. positive (either)	1.01 (0.91 – 1.12)	1.11 (0.98 – 1.26)
	Unknown or borderline (both) vs. positive (either)	0.88 (0.73 – 1.07)	1.04 (0.80 – 1.36)
Lymph node (LN) status	LN positive vs. LN negative	0.67 (0.60 – 0.74)	0.97 (0.83 – 1.12)
Neighborhood quintile of socioeconomic status (SES)	Second lowest (2) vs. lowest (1)	1.03 (0.88 – 1.21)	1.21 (0.97 – 1.50)
	Middle (3) vs. lowest (1)	1.06 (0.90 – 1.23)	1.66 (1.34 – 2.05)
	Second highest (4) vs. lowest (1)	1.03 (0.88 – 1.21)	1.58 (1.27 – 1.96)
	Highest (5) vs. lowest (1)	1.07 (0.90 – 1.27)	2.10 (1.67 – 2.64)
Marital status	Not married vs. married	0.89 (0.81 – 0.98)	1.03 (0.92 – 1.17)
	Unknown vs. married	0.84 (0.65 – 1.08)	0.62 (0.43 – 0.88)
SES distribution of patients treated in reporting hospital	Mixed distribution vs. >50% high SES	0.96 (0.85 – 1.08)	0.77 (0.65 – 0.90)
	>50% low SES vs. >50% high SES	0.80 (0.68 – 0.94)	0.54 (0.43 – 0.68)
Primary insurance	Medicare vs. private	0.99 (0.79 – 1.26)	0.93 (0.68 – 1.27)
	Military vs. private	1.23 (0.80 – 1.90)	1.01 (0.58 – 1.78)
	Not insured or self-pay vs. private	0.74 (0.50 – 1.09)	0.75 (0.45 – 1.28)
	Public or Medicaid vs. private	0.84 (0.74 – 0.94)	0.60 (0.51 – 0.70)
	Unknown vs. private	0.85 (0.65 – 1.11)	0.54 (0.36 – 0.82)
Reporting hospital was National Cancer Institute-designated cancer center	Yes vs. No	1.28 (1.10 – 1.49)	0.85 (0.69 – 1.05)
Year of diagnosis	2012 vs. 1998	2.14 (1.60 – 2.87)	8.66 (5.38 – 13.9)

*OR, odds ratio; CI, confidence interval